

Male Breast Cancer: A Retrospective Study From a Regional Cancer Center in Northern India

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Over a 7-year period from 1987 to 1993, 41 male breast cancer patients were seen in the breast cancer clinic of the Institute Rotary Cancer Hospital (IRCH) at the All India Institute of Medical Sciences (AIIMS). Their mean age was 54.2 years; and duration of symptoms ranged from 1 to 84 months with a mean of 15.1 months. Breast lump was the commonest presenting symptom. Fine needle aspiration cytology (FNAC) was the commonest diagnostic procedure. The TNM stage distribution was stage I, 5; stage II, 13; stage III, 17; and stage IV, 6. Radical mastectomy (25/36) was the commonest surgical procedure. Locoregional radiotherapy was given in 15 patients. Thirty patients received systemic adjuvant therapy (chemotherapy or tamoxifen, or a combination of the two). Local or distant recurrence occurred in 8 patients (8/31, 28.3%). Actuarial overall and disease-free survival was 100% and 80.1% at 2 years and 91.7% and 66.7% at 4 years, respectively. On univariate analysis, axillary lymph node status and age were found to affect disease-free survival significantly. Advanced stage of disease at presentation is common in Indian patients and will continue to influence treatment policies. Neoadjuvant chemotherapy needs to be evaluated for locally advanced tumors to improve outcome. Multicentric studies are necessary to define the relative roles of tamoxifen and chemotherapy for adjuvant treatment. © 1996 Wiley-Liss, Inc.

KEY WORDS: tamoxifen, adjuvant chemotherapy, radiotherapy

INTRODUCTION

Breast cancer in men is a rare disease [1]. In data from various cancer centers, male breast cancer constitutes less than 1% of all male cancers, and its incidence is roughly 1% of female breast cancer. The age-adjusted incidence rates for male breast cancer in the Delhi and Bombay cancer registries [2] were 0.3 and 0.4 per 100,000, respectively, in the year 1988. During the same period, incidence rates for female breast cancer were 26.2 and 25.0 per 100,000 for Delhi and Bombay, respectively [2].

Because of its rarity, the biological behavior of the disease is not well known, and there are no definite guidelines regarding the optimal therapeutic approach. The

trend world wide is to treat it in a fashion similar to female breast cancer. We have not come across any published series of male breast cancer from India. This prompted us to do a retrospective review of our male breast cancer patients.

MATERIALS AND METHODS

This study was carried out at the Institute Rotary Cancer Hospital (IRCH), New Delhi. IRCH is a tertiary cancer

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care center of northern India. Nearly 500 new cases of female breast cancer are registered in the breast cancer clinic at IRCH every year. The current study is a retrospective review of 41 patients of male breast cancer seen over a 7-year period from 1987 to 1993. Some of these patients had been treated before being referred to IRCH.

Records of these patients were studied for clinical features, diagnostic procedures used, stage at presentation (TNM staging), treatment received and follow-up. Patients not coming for regular follow-up were contacted through letters. Follow-up information was available for 33 patients (complete follow-up in 30 and partial in 3). Actuarial overall and disease free survival analysis and univariate analysis of prognostic factors (age, duration of illness, nodal status, and the TNM stage) were carried out using the Kaplan-Meier product limit method [3].

RESULTS

Mean age at diagnosis was 54.2 years (SD 11.3 years) with a range of 28 to 74 years. The majority of patients (36/41) were in the age range of 40–70 years. The duration of symptoms ranged from 1 to 84 months (mean 15.1 months, median 7 months). The presenting symptom was a breast lump in all patients (100%), which was left-sided in 24 (58.5%). The lump was subareolar in 35 (85.4%), in the upper outer quadrant (UOQ) in 5 (12.2%), and in the upper inner quadrant in one. Other features were nipple discharge (7/41, 17.1%), nipple retraction (6/41, 14.6%), Paget's disease (3/41, 7.3%), ulceration (6/41, 14.6%), and peau d'orange (6/41, 14.6%). The tumor size ranged from 0.5 to 6 cm (<2 cm in 11 patients, 2–5 cm in 22 patients, >5 cm in 8 patients). Axillary lymph nodes and supraclavicular lymph nodes were enlarged in 22 and in 3 patients, respectively.

Information on risk factors was available in 17 patients. Family history of female breast cancer and history of chronic liver disease was present in one each. History of significant head injury was present in two patients. None (0/17) had history of radiation exposure, estrogenic drug intake, orchitis, orchidectomy or Klinefelter's syndrome. Gynecomastia was found on examination in 6 of the 41 patients (14.6%).

Fine-needle aspiration cytology was the commonest diagnostic investigation, but excision or incision biopsy was used in nearly 40% of cases (many patients underwent an excision or incision biopsy before attending IRCH). Frozen section examination was necessary in only one patient. Radical mastectomy was the commonest surgical procedure performed (25/36; Table I). The most common histologic type was infiltrating duct carcinoma (39/41). The remaining two had papillary carcinoma. Overall TNM status is listed in Table II. Only one patient had a T3 tumor, while the tumor size was >5 cm in eight patients, suggesting that most tumors involved the skin by the time they reached this size. Two tumors of 2-cm

TABLE I. Type of Surgery for Male Breast Cancer

Type of mastectomy	N	%
Radical	25	69.5
Modified radical	4	11.1
Simple	4	11.1
Lumpectomy	3	8.3
Total:	36 ^a	

^a Five of the 41 patients had no surgery.

TABLE II. TNM Status and TNM Stage Group in 41 Patients With Male Breast Cancer

T status	N	N status	N	M status	N
T1	9	N0	16	M0	35
T2	11	N1	19	M1	6
T3	1	N2	6		
T4 ^a	20				
TNM stage					
Stage I	5	Stage II	13		
Stage III	17	Stage IV	6		

^a Nineteen of these were T 4b and 1 was T 4c.

TABLE III. Sites of Distant Metastasis for Male Breast Cancer at Initial Presentation and Recurrence

Site	At initial presentation ^a	On disease recurrence ^b
Bone	4	4
Lung	1	4
Liver	0	1
Liver	0	1
Brain	0	1
SCLN ^c	3	0

^a Six patients with a total of 8 sites of involvement.

^b Seven patients with a total of 10 sites of involvement.

^c Supraclavicular lymph node(s).

size also had skin involvement (T4b). Based on TNM stage grouping (Table II), 23 patients had advanced disease at presentation (stages III and IV, 56.1%). The sites of distant metastasis in stage IV patients are listed in Table III.

Thirty of the 36 operated patients received some form of adjuvant therapy. Seventeen patients had single modality treatment [chemotherapy (CT)-7, radiotherapy (RT)-4, tamoxifen (HT)-5, orchidectomy-1]. Combined modality treatment was used in 13 patients (RT and HT, 6; CT, HT, and RT, 4; CT and HT, 2; CT and RT, 1).

For 31 patients (after excluding stage IV and patients lost to follow-up), follow-up periods ranged from 12 to 183 months (mean 41.8 months, median 30 months). Local and/or distant recurrence was noted in 8 patients (28.3%). Recurrence was local in one, distant in three, and combined in four patients. Of the four patients with

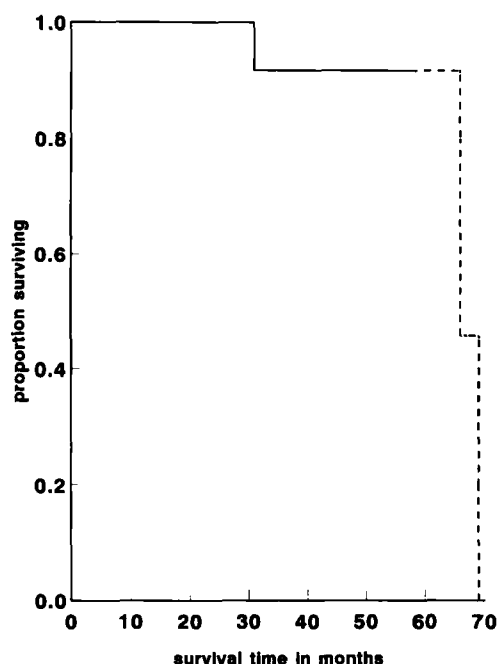


Fig. 1. Actuarial Kaplan-Meier plot of overall survival of male breast cancer following treatment (28 patients, 25 censored).

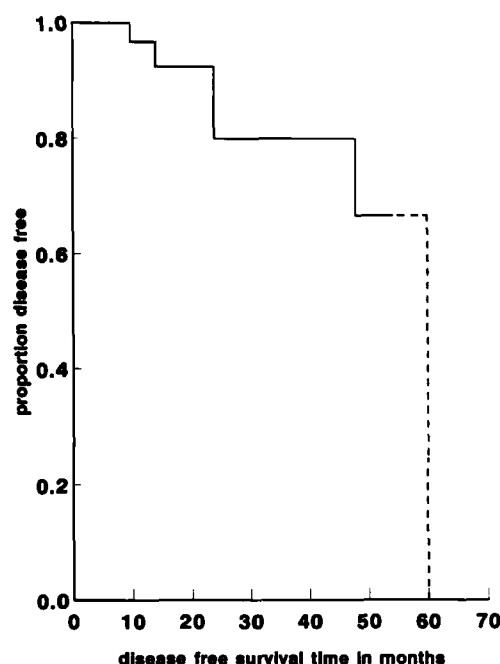


Fig. 2. Actuarial Kaplan-Meier plot of disease-free survival of male breast cancer following treatment (28 patients, 22 censored).

both local and distant recurrence, two had local recurrence first, and two had synchronous recurrence. Mean interval for local and distant recurrence were 31.4 and 60.7 months, respectively). The sites of distant recurrence are presented in Table III. Local recurrence was treated with radiotherapy in 3 patients and combined modality therapy (CT, RT, HT) in two with synchronous distant recurrence. Orchidectomy was carried out in three of the patients with distant recurrence.

Three patients had their primary surgery 1–8 years before coming to IRCH. Their follow-up periods were 90, 120, and 183 months. Excluding these three patients, the follow-up period for the remaining 28 patients ranged from 12 to 69 months (mean 32.25; median 26.5 months). The TNM stage distribution of these 28 patients was stage I, 5; stage II, 9; stage III, 14. Using the Kaplan-Meier product limit method, overall mean survival was 64.6 months (SE 3.76, median 66). The mean disease free survival was 50.33 months (SE 4.14, median 60). The actuarial overall (Fig. 1) and disease-free survival (Fig. 2) at 2 years were 100% and 80.1%, respectively; the same at 4 years were 91.7% and 66.7%, respectively. The results of univariate analysis are presented in Table IV. Axillary lymph node status and age (Figs. 3, 4) were the two factors found to affect the actuarial disease-free survival significantly.

DISCUSSION

The mean age in the current series (54.2 years) is less than the mean age reported by Crichlow [1] (59 years),

Borgen et al. [4] (61 years) and Guinee et al. [5] (62.8 years). It is comparable to 54 years reported by Ihekwa [6] from Nigeria. The lower mean age in our series, as well as the African data, may be due to the age structure of the respective populations. Age range is wider in the Western series (Borgen et al. [4], 25–83 years; Guinee et al. [5], 23–97 years). The oldest patient in our series was 74 years and 80 years in the Nigerian series [6]. This could be responsible for some of the observed difference in mean age. Mean age at presentation in men has been found to be 6–11 years more than in women [1]. The mean age of female breast cancer patients in our clinic [7] was 46.8 years with a range of 22–70 years, confirming this observation.

Of the various risk factors for male breast cancer, gynecomastia is one of the most controversial. It is often associated with male breast cancer [8], but a causative relationship has not been shown. Borgen et al. [4] found clinical gynecomastia in 23% of their patients (14.5% in the current study). Microscopic evidence of gynecomastia is more common [8]. History of head injury, present in 2 of the 17 patients in the current series, has been proposed as a risk factor for male breast cancer by Olsson and Ranstam [9]. These investigators found a history of head injury to be significantly more common in male breast cancer than in lymphoma and lung cancer. They suspect it to be acting through hyperprolactinemia.

The higher incidence in the left breast, 58.5% vs. 41.5% in the right breast in this study, has been observed before and is unexplained [10]. The presenting features in our

TABLE IV. Prognostic Factors for Male Breast Cancer

Prognostic factors	Disease-free survival (months)			Overall survival (months)		
	Mean	(SE)	P	Mean	(SE)	P
Age (years)						
≤50	40.2	(6.4)	<0.05	63.6	(7.1)	NS
>50	60.0	(0.0)		66.0	(0.0)	
Duration						
≤6 mo	51.1	(4.6)	NS	64.8	(5.6)	NS
>6 mo	46.7	(7.3)		66.0	(0.0)	
N status						
Negative	57.0	(0.0)	<0.05	57.0	(0.0)	NS
Positive	44.1	(5.8)		62.3	(6.0)	
TNM stage						
I/II	50.7	(3.2)	NS	54.0	(0.0)	NS
III	47.3	(6.0)		62.3	(6.0)	

NS, not significant; $P > 0.05$.

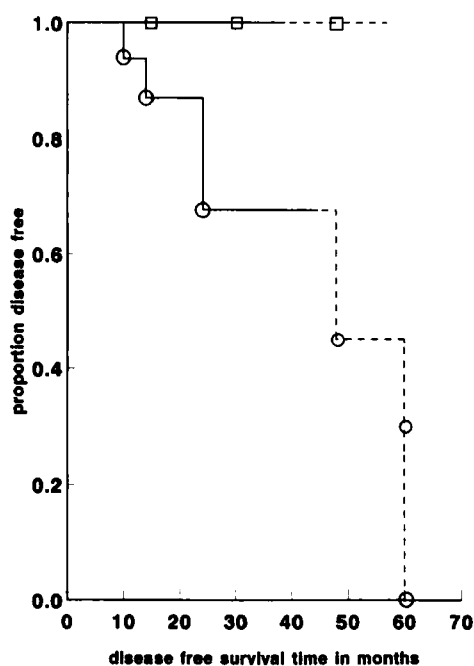


Fig. 3. Actuarial Kaplan-Meier plot of disease-free survival of male breast cancer as a function of axillary lymph node status (node positive: \circ , 16 patients, 10 censored; node negative: \square , 12 patients, 12 censored).

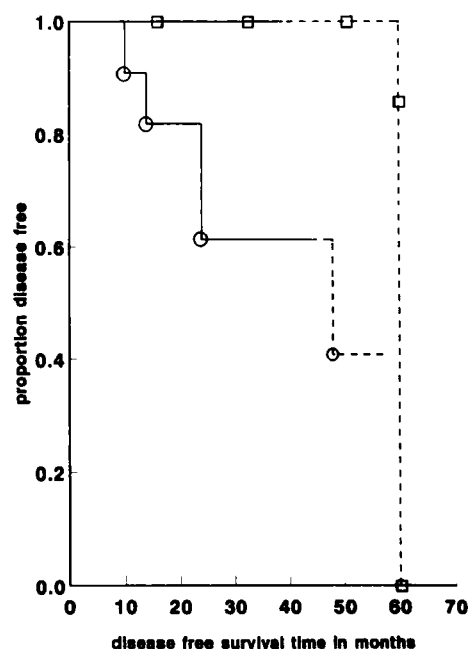


Fig. 4. Actuarial Kaplan-Meier plot of disease-free survival of male breast cancer as a function of age of the patients (age ≤ 50 years: \circ , 11 patients, 6 censored; age > 50 years: \square , 17 patients, 16 censored).

series are similar to previous observations [4,10,11], with a painless subareolar lump the commonest. Mean delay in presentation (15.1 months) in our series is significantly longer than that reported by Borgen et al. [4] (5 weeks) but is in line with older reports from the West [1,12] (10–18 months) and a report from Nigeria [6] (16.4 months). This delay is longer than that observed in females in our setup [7] (mean delay of 11.3 months). Nearly 30% of male patients had a delay of more than 1 year, compared to 23% of females. Similar data have been reported by Mausner et al. [13].

The study of TNM status showed one interesting feature. Although there were eight patients with a tumor size of more than 5 cm, there was only one T3 tumor. This finding suggests that most of the lesions in males involve the skin (become T4) by the time they attain a size of more than 5 cm. Historically, male breast cancer presented in a more advanced stage than female breast cancer [1,13]. However, the TNM stage distribution in the current study is comparable to the data for female patients in our clinic [7]: stage I, 7.3%, stage II, 22.3%, stage III, 52.4%, stage IV, 18%. In two African series [6,14], a high proportion of cases had advanced disease (stage III or IV) at presenta-

tion. By contrast, Borgen et al. [4] found 77% of patients (after excluding stage IV) to have early disease (stage 0/I/II). In their series as well, the stage distribution was similar to that of female breast cancer.

Surgery forms the mainstay of therapy. Radical mastectomy (RM) was the commonest procedure in our series. It has been the procedure of choice for male breast cancer based on the belief that the smaller amount of breast tissue in males would lead to a higher rate of local recurrence if less radical surgery (modified radical mastectomy, MRM) is done. However, in Western series [4], MRM is now the commonest procedure. This change in trend is due to an earlier stage at presentation and the realization that RM is not superior to MRM in female patients.

Published literature shows great variation in the use of postoperative RT (Borgen et al [4]: 3/92; Guinee et al. [5]: 245/208; Engin and Unsal [14]: 20/21). In the current series, 15 patients received locoregional RT (stage III, 10, stage I/II, 5). Irradiation of the chest wall may be avoided in T1/T2/T3 lesions without increasing the risk of local recurrence. Crichlow and Galt [10] have recommended that RT to the internal mammary nodes should be considered in all cases, as the tumors are mostly centrally located, and the risk of internal mammary node involvement is high.

Systemic adjuvant therapy is used in node-positive male breast cancer patients because survival advantage has been observed in female patients with such therapy. Adjuvant chemotherapy was given to 14 patients and tamoxifen to 17 patients in the current study. However, the relative roles of tamoxifen and chemotherapy have not been defined. In two studies of adjuvant chemotherapy [15,16] in stage II/III male breast cancer, estimated 5-year survival was reported to be 80–85%. In a study of adjuvant Tamoxifen by Ribeiro and Swindell [17], there was a significant survival advantage for patients treated with tamoxifen. There are no studies comparing the efficacy of tamoxifen and chemotherapy in adjuvant setting. In female patients, menopausal and receptor [estrogen (ER), progesterone (PR)] status are used as guidelines for planning adjuvant therapy. There is no equivalent of menopausal status in males; thus, receptor status is the only potential indicator. Hormonal therapy could play a greater role in males, as the receptor positivity rate is higher in male breast cancer (ER positive 38/43, PR positive 32/42, Borgen et al. [4]; ER and PR positive 12/16, Ribeiro [18]).

Neoadjuvant therapy may have a significant role in male breast cancer management as a large number of cases seen in our setup are locally advanced. We have recently used neoadjuvant chemotherapy in four patients, but it is too early to assess the results.

The actuarial overall and disease-free survival rates at 4 years were 91.7% and 66.7%, respectively. Borgen et al. [4] reported 5-year overall and disease-free survival

rates of 85% and 68%, respectively. Engin and Unsal [14] reported 5-year overall and disease-free survival of 37% and 27%, respectively but these results included stage IV patients as well. Crichlow [1] has reported a 5-year overall survival rate of 49% in a collective review in 1972. The outcome of male breast cancer has improved compared to that time period. On univariate analysis, age at presentation and axillary lymph node status were found to influence disease-free survival significantly in our series. The results for overall survival were unclear, possibly a reflection of the shorter follow-up and the lesser number of patients. Axillary node involvement has been found to be the most important prognostic factor by all investigators [4,5,10,11,14]. Node-negative patients have significantly better survival (5 year overall figures of 77–100%) than node-positive patients (5 year overall survival of 46–60%). A relationship with number of positive nodes has also been reported by Guinee et al. [5]. In our study also, node-negative patients had significantly better survival (median disease-free survival DFS, 57 months) than node-positive patients (median DFS, 48 months). Increasing age has been reported to worsen prognosis in a study of 1,429 patients from four Nordic countries [19]. Engin and Unsal [14] also found the prognosis to be worse in patients older than 60 years, while no significant difference was noted by Borgen et al. [4]. In our study, patients under 50 years of age had a shorter disease-free survival than that of patients older than 50. We used a dividing line of 50 years, as the mean age in our series is less than in the Western literature. Using 60 years as the dividing line, the difference was not statistically significant. The TNM stage did not affect the observed survival significantly in the current study. This may be a reflection of the shorter follow-up period in our study. Borgen et al. [4] also observed that the survival curves for stage II and III patients were similar initially and the survival differences manifested only after a follow-up of 90 months.

CONCLUSIONS

As is true of female breast cancer, patients with male breast cancer in India also present with advanced disease, and this will continue to influence our treatment policies. This is due to delay in presentation (which is more than the delay for female patients at our center). The mean age of our patients is nearly 10 years less than patients in the West. Medium-term survival (at 4 years) figures in our patients are comparable to those reported by Borgen et al. [4], but it is difficult to comment on the long-term outcome as our follow-up period is shorter. Axillary lymph node status and age were the two determinants of survival on univariate analysis.

Stage for stage, current management of male breast cancer is generally similar to female breast cancer, except for breast conservation. Areas for further study in male

breast cancer are role of neoadjuvant chemotherapy in locally advanced disease, role of locoregional RT for the chest wall and the internal mammary lymph nodes, the relative role of tamoxifen and chemotherapy in systemic adjuvant treatment. In view of the rarity of this disease, multicentric studies are necessary for meaningful results.

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